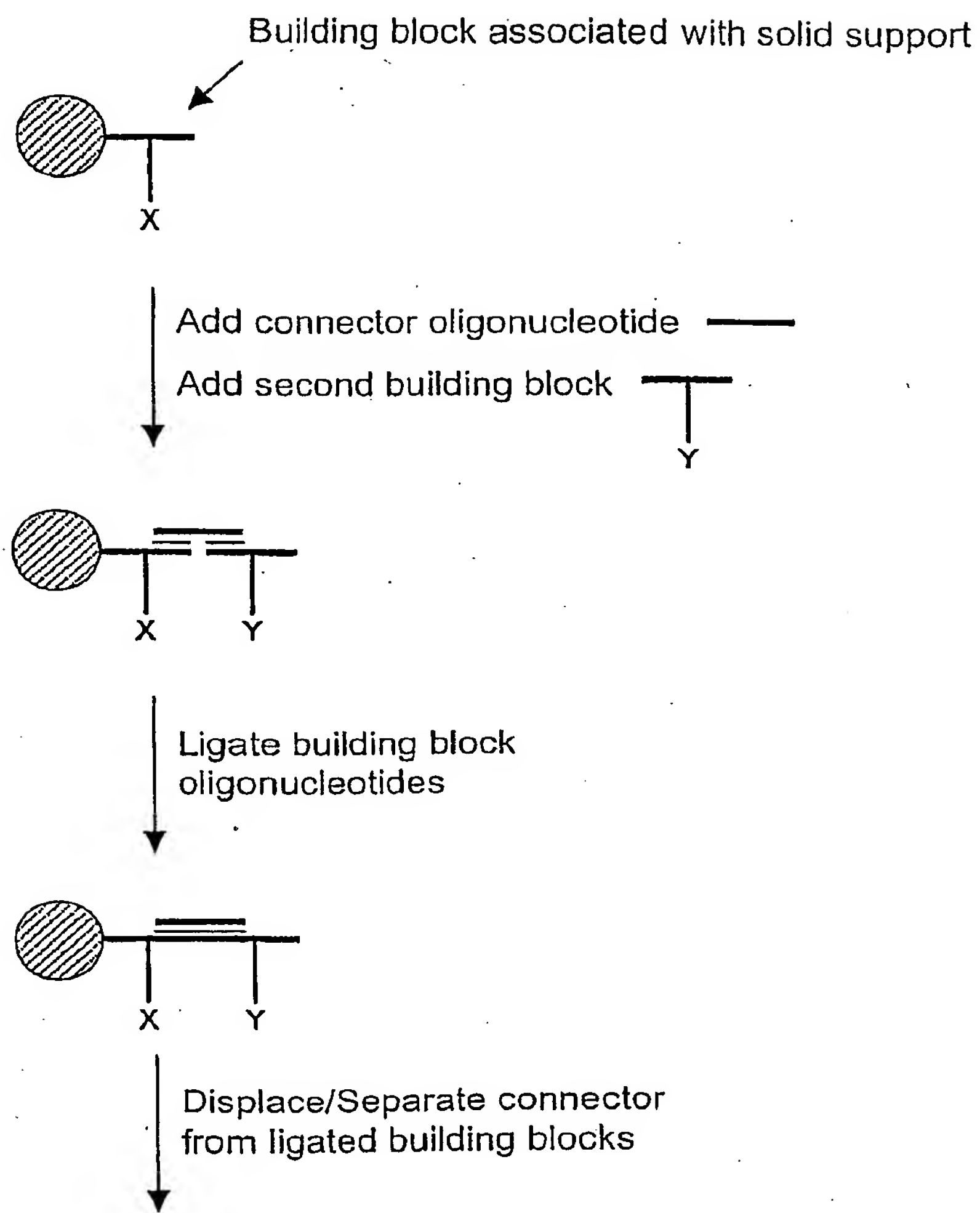
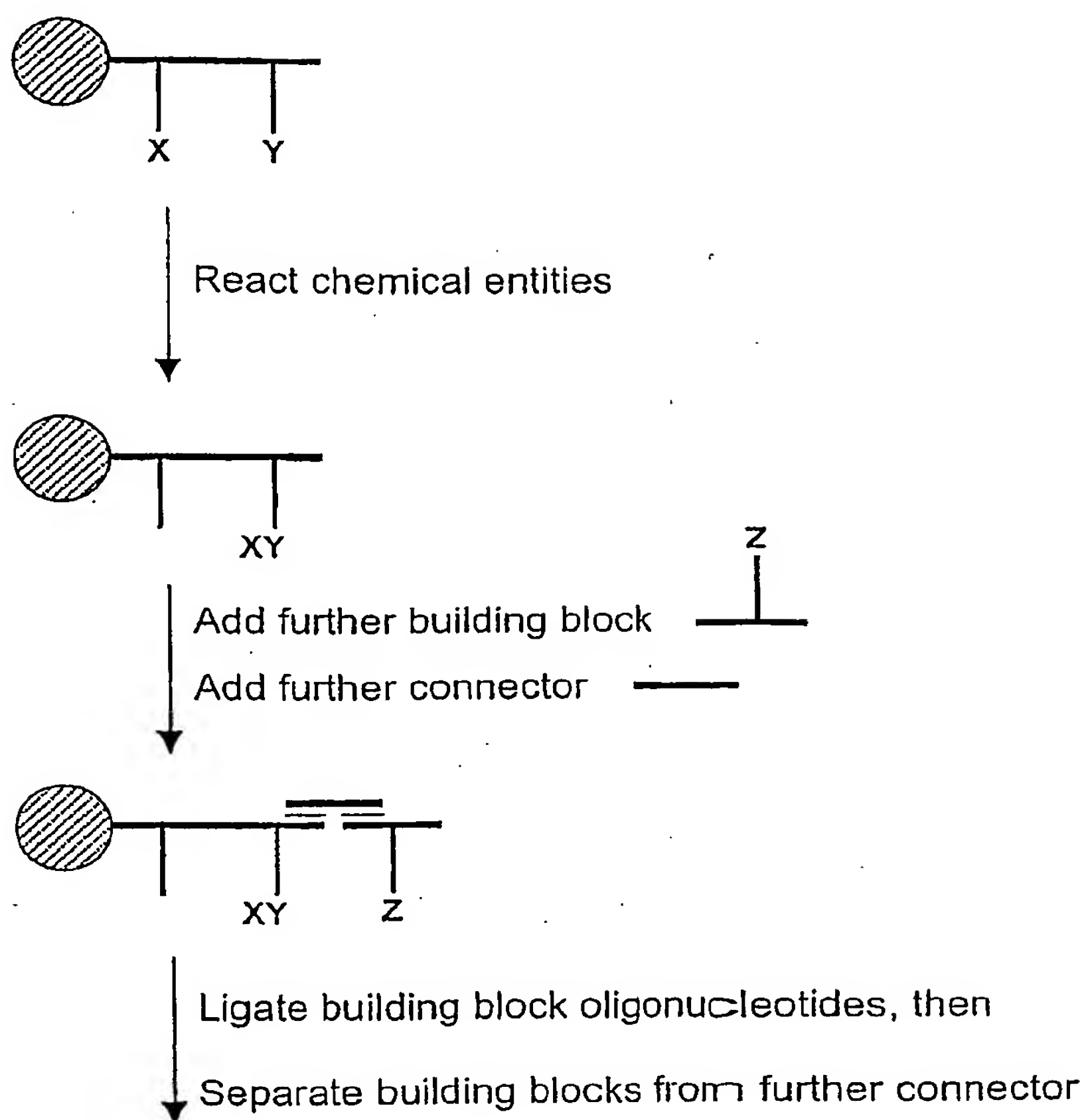


1/32

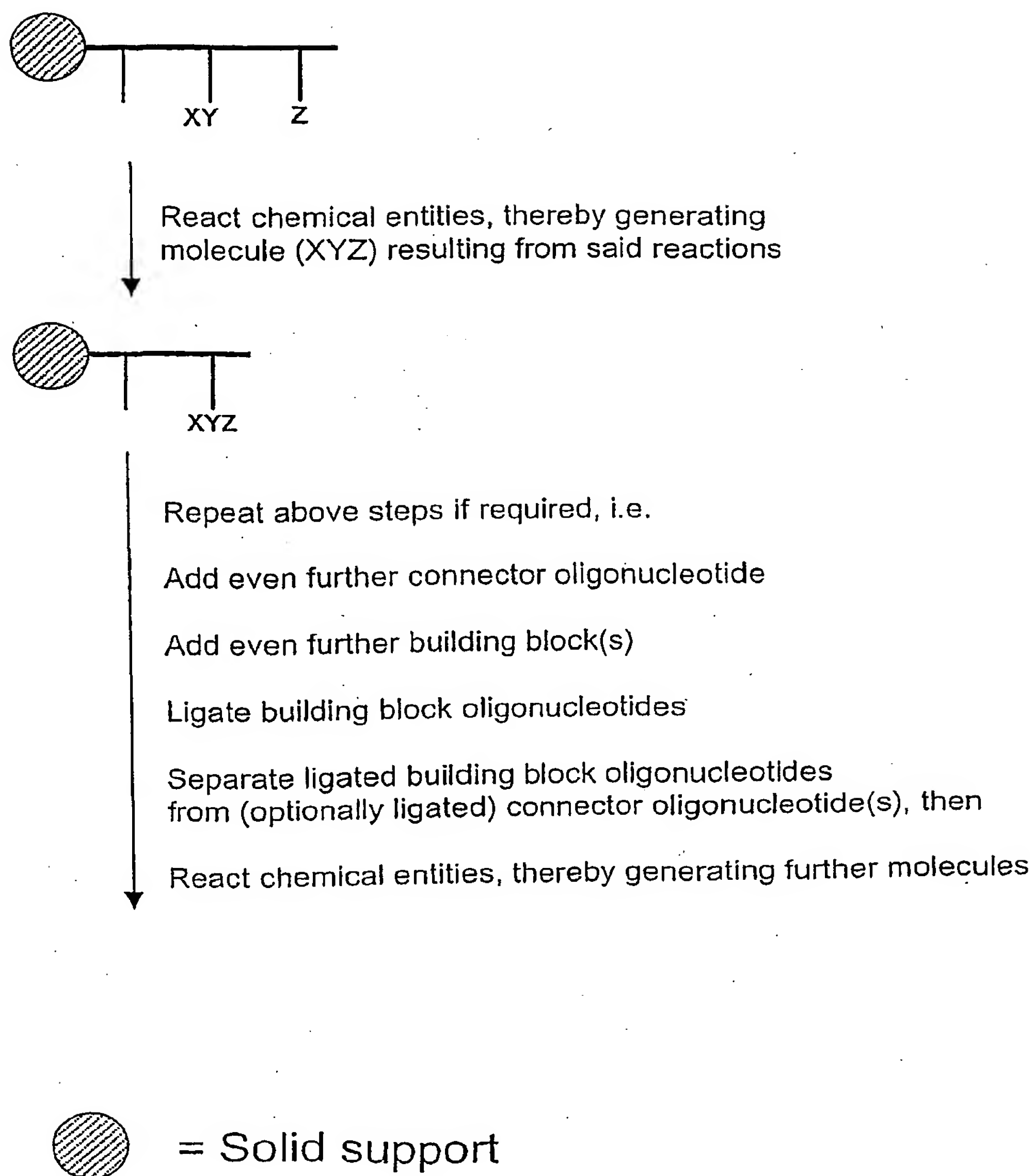
Figure 1A = Solid support

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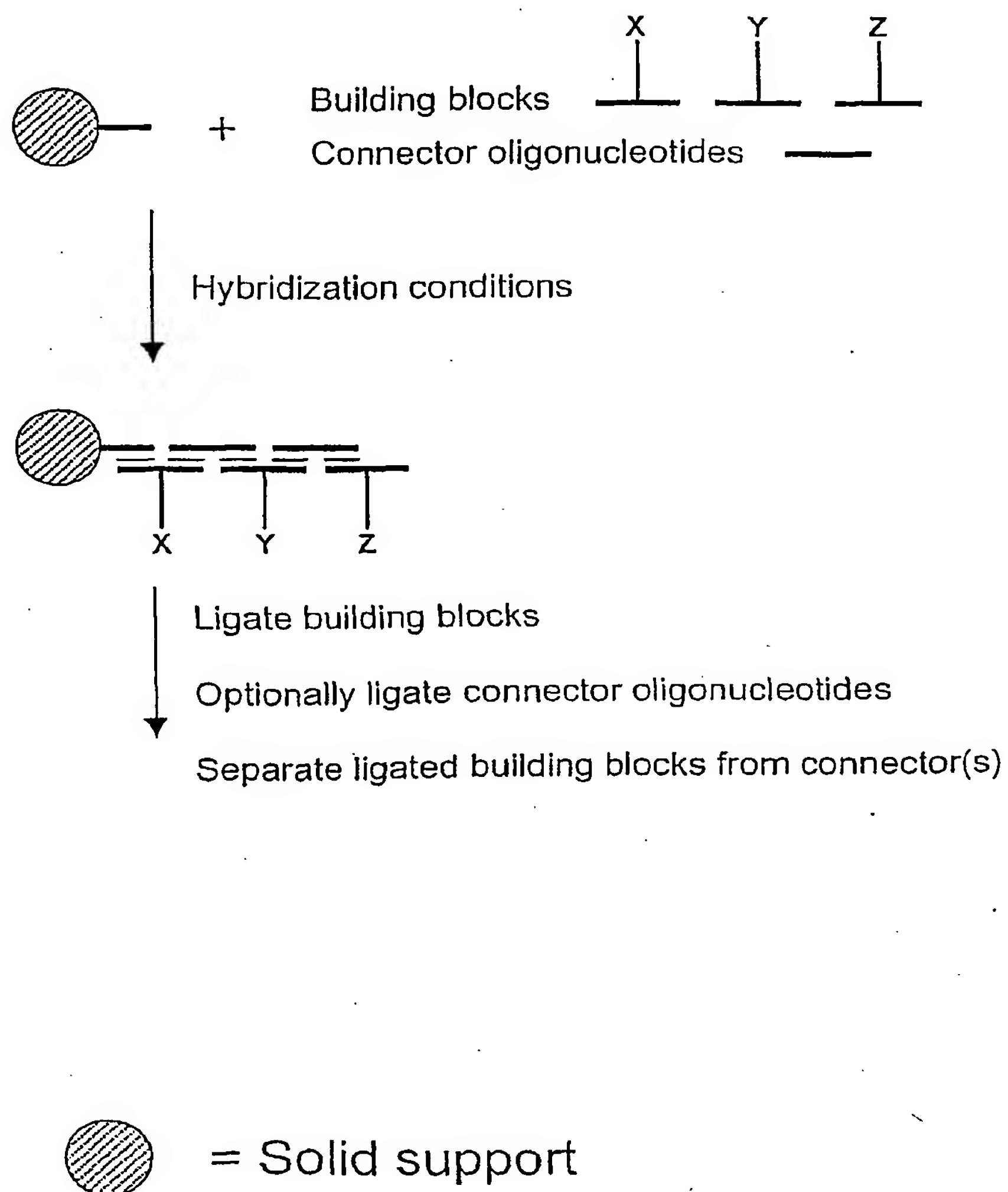
Figure 1B

 = Solid support

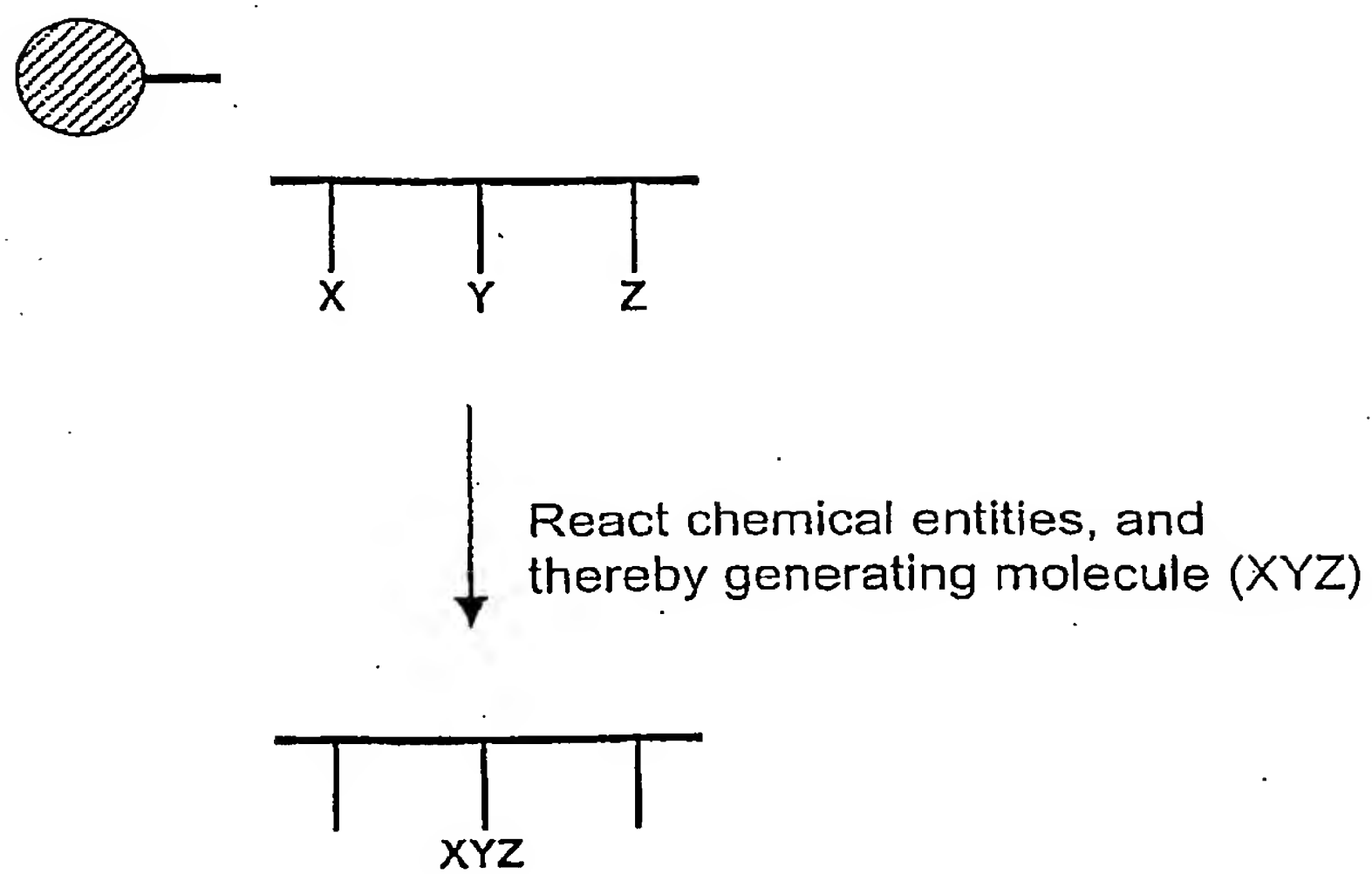
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Figure 1C

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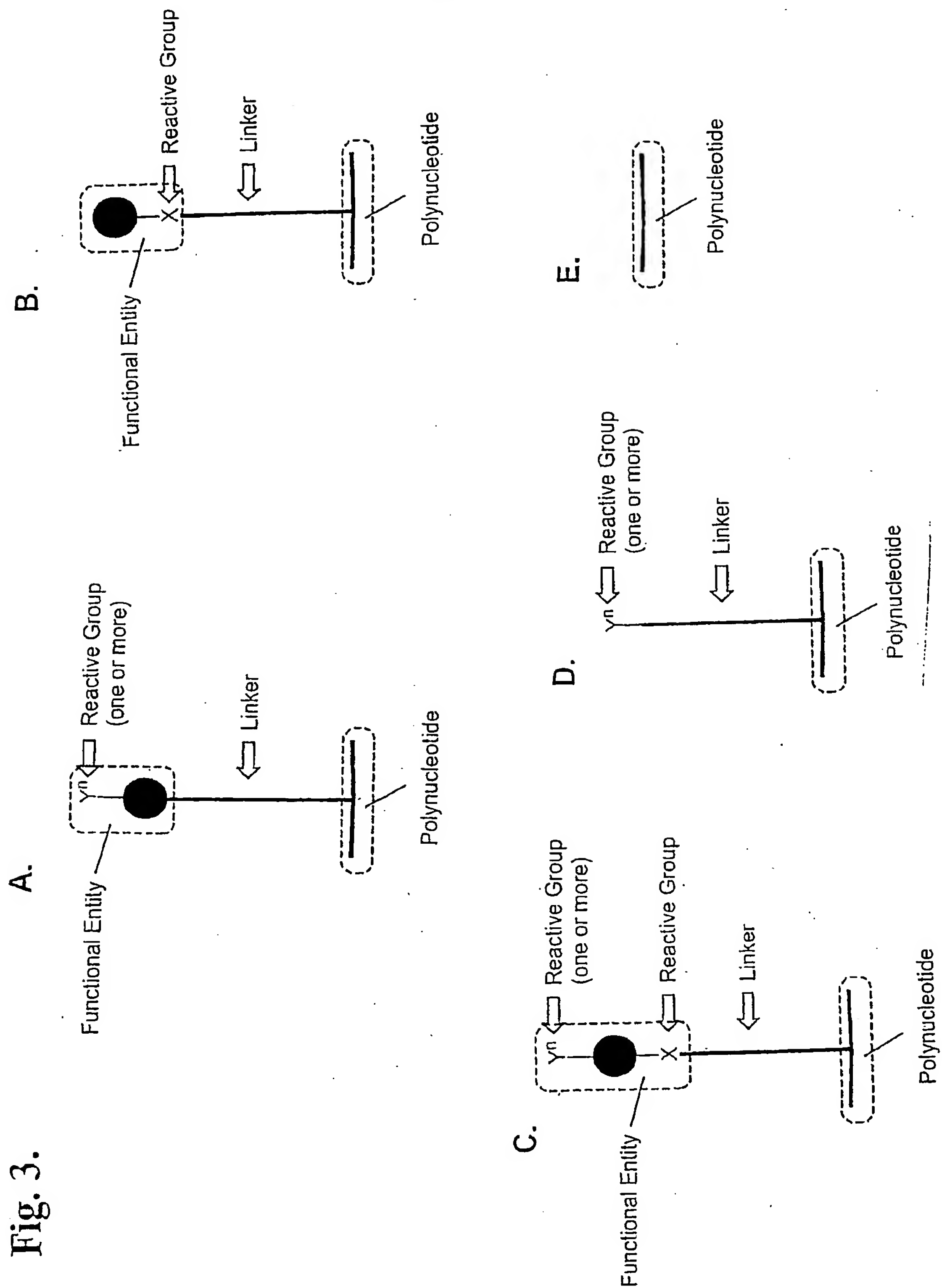
Figure 2A

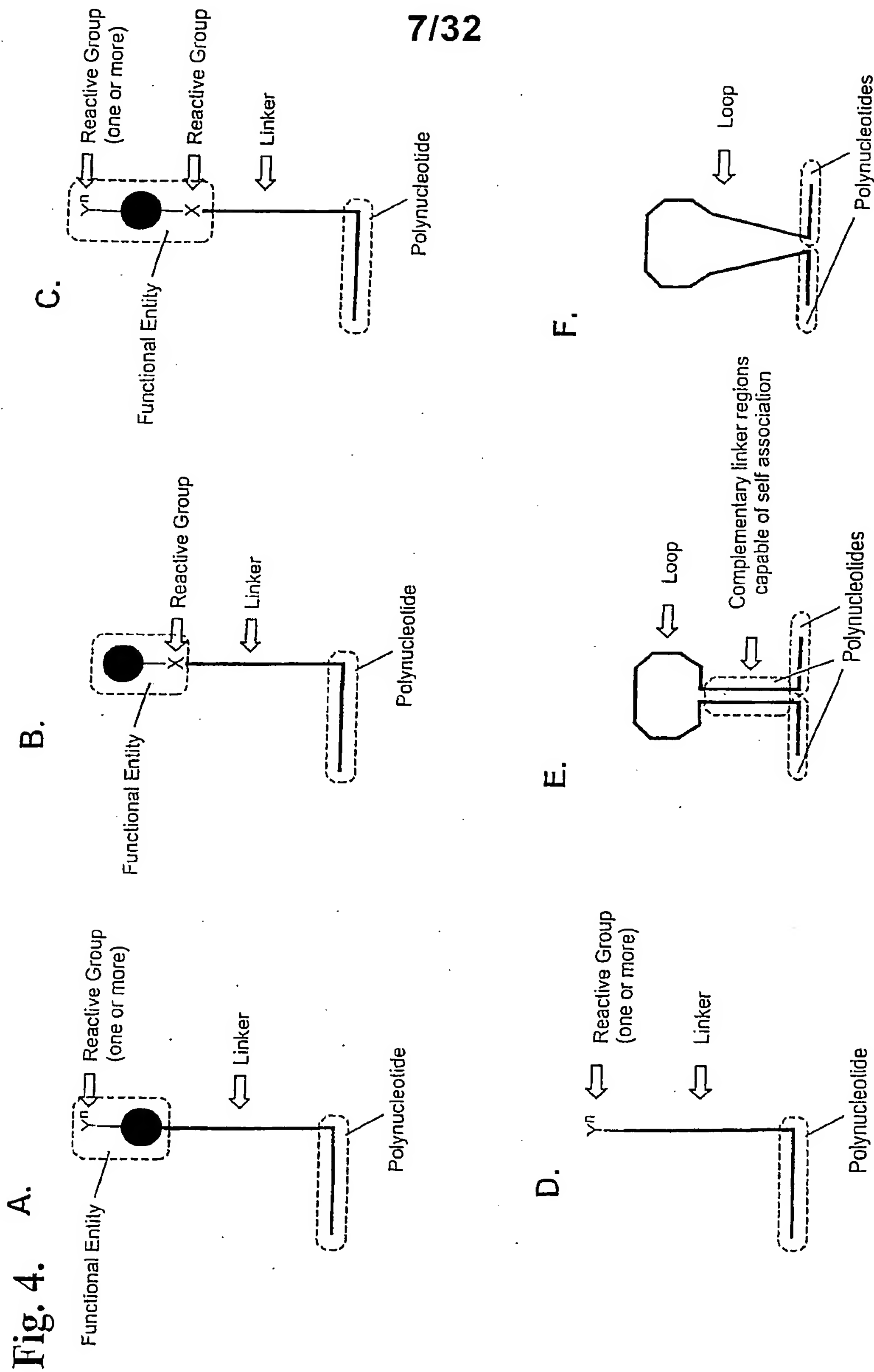
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Figure 2B = Solid support

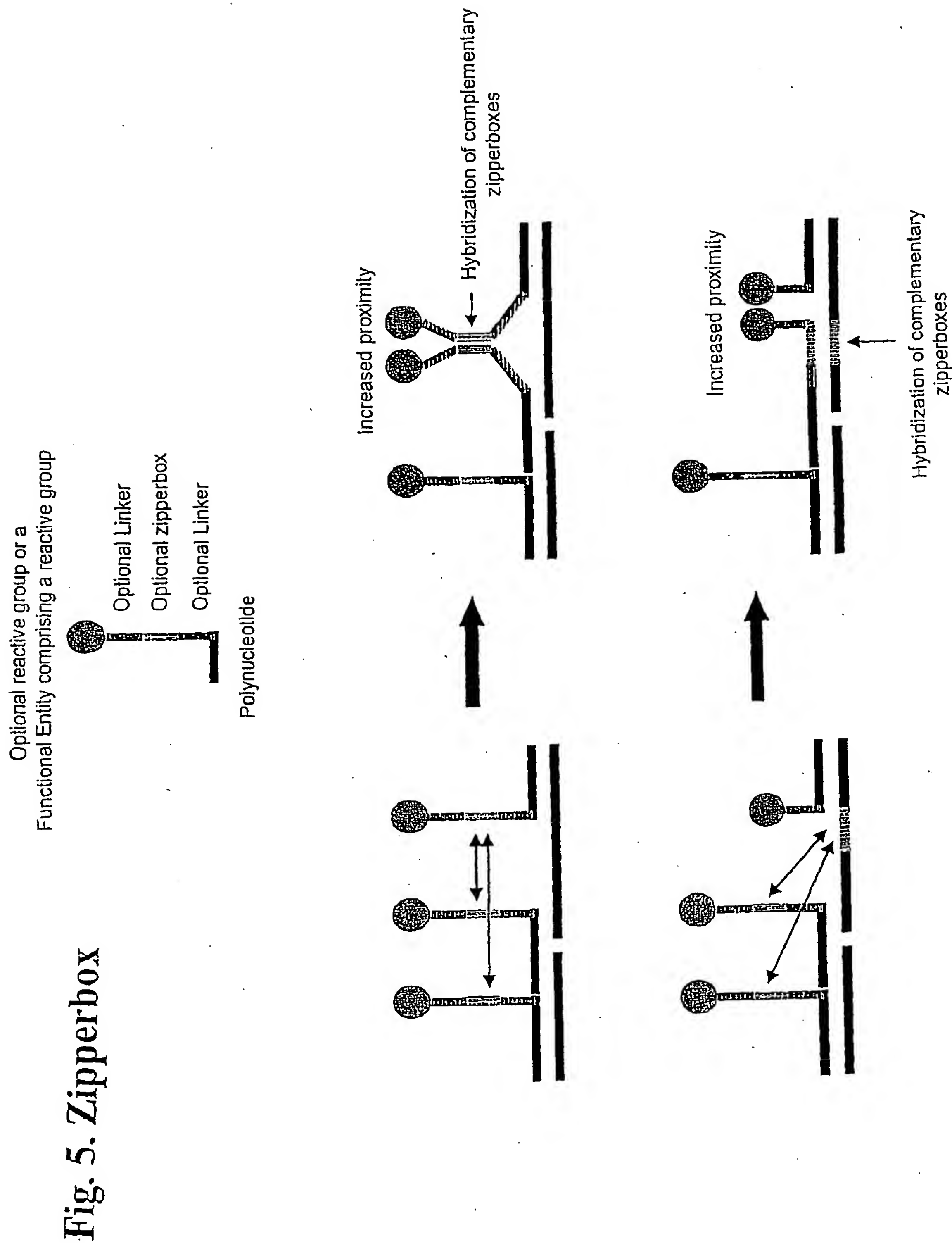
6/32

Fig. 3.

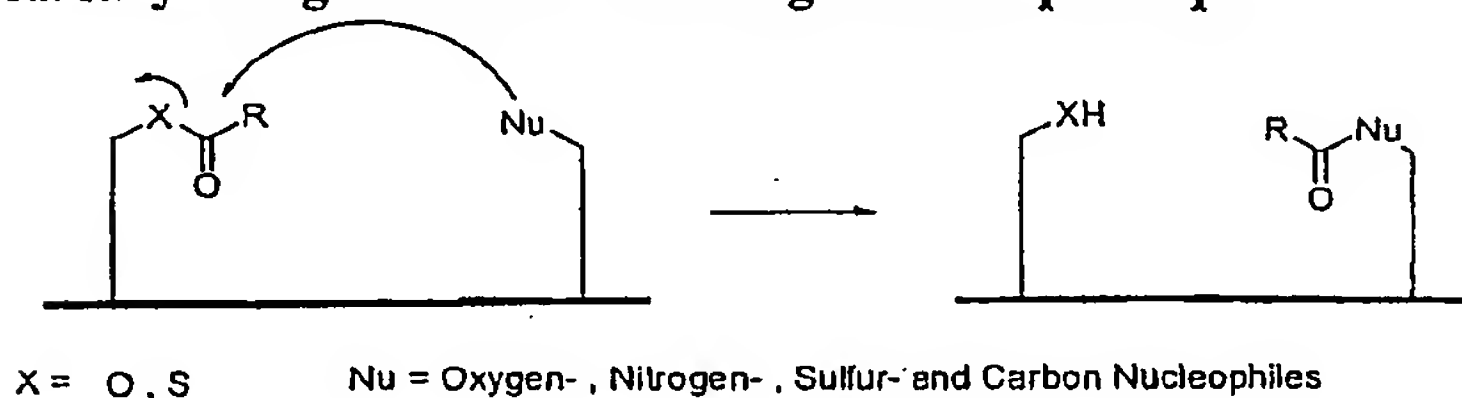




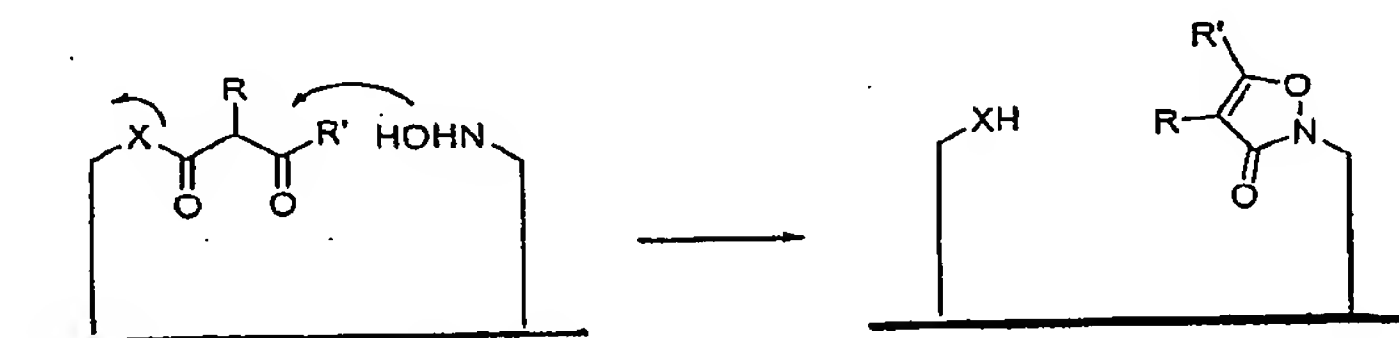
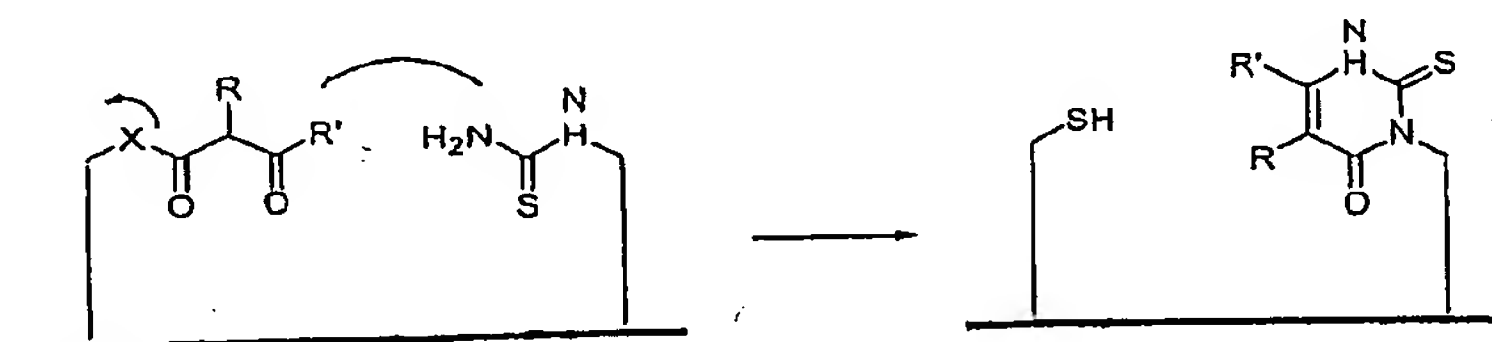
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Fig. 6. Reaction types allowing simultaneous reaction and linker cleavage.**Nucleophilic substitution using activation of electrophiles****A. Acylating monomer building blocks - principle****B. Acylation****Amide formation by reaction of amines with activated esters****C. Acylation****Pyrazolone formation by reaction of hydrazines with β -Ketoesters**

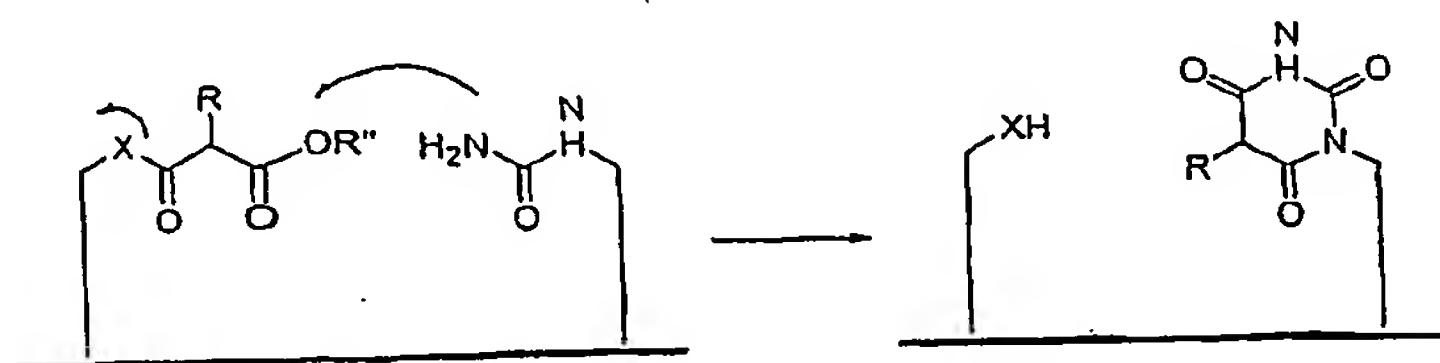
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**D. Acylation**Isoxazolone formation by reaction of hydroxylamines with β -Ketoesters**E. Acylation**Pyrimidine formation by reaction of thioureas with β -Ketoesters**F. Acylation**

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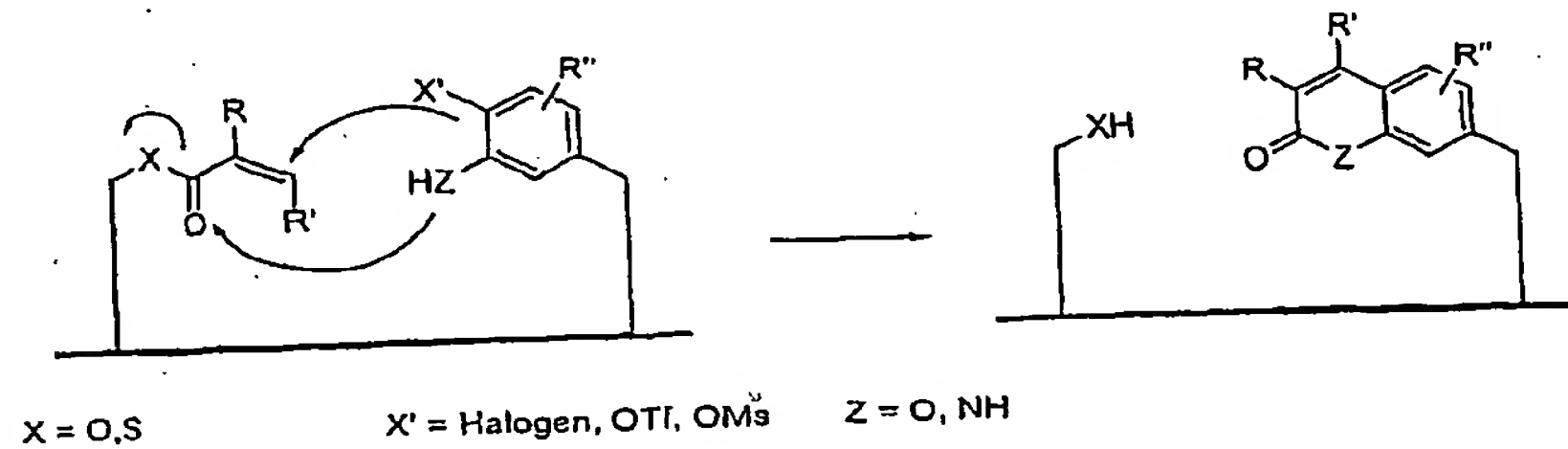
11/32

Pyrimidine formation by reaction of ureas with Malonates



G. Acylation

Coumarine or quinolinon formation by a Heck reaction followed by a nucleophilic substitution

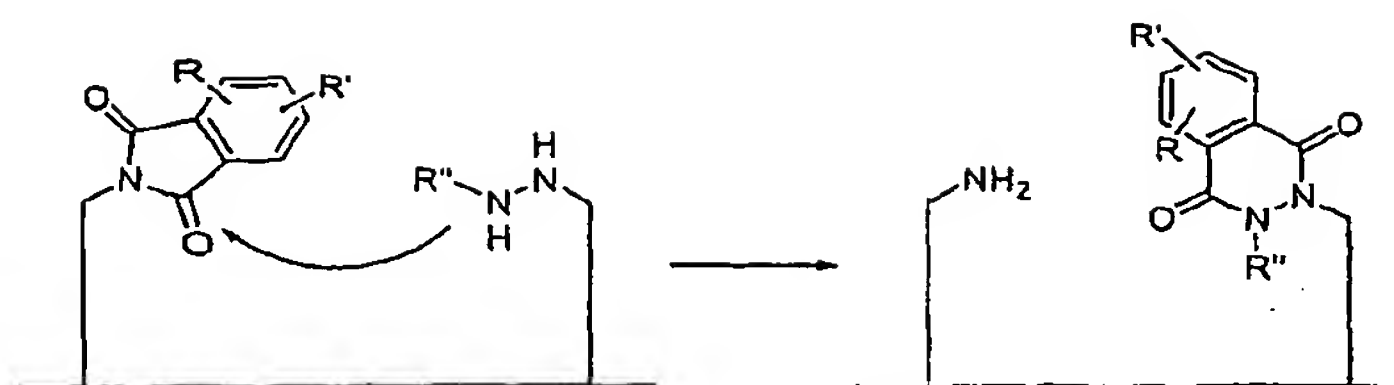
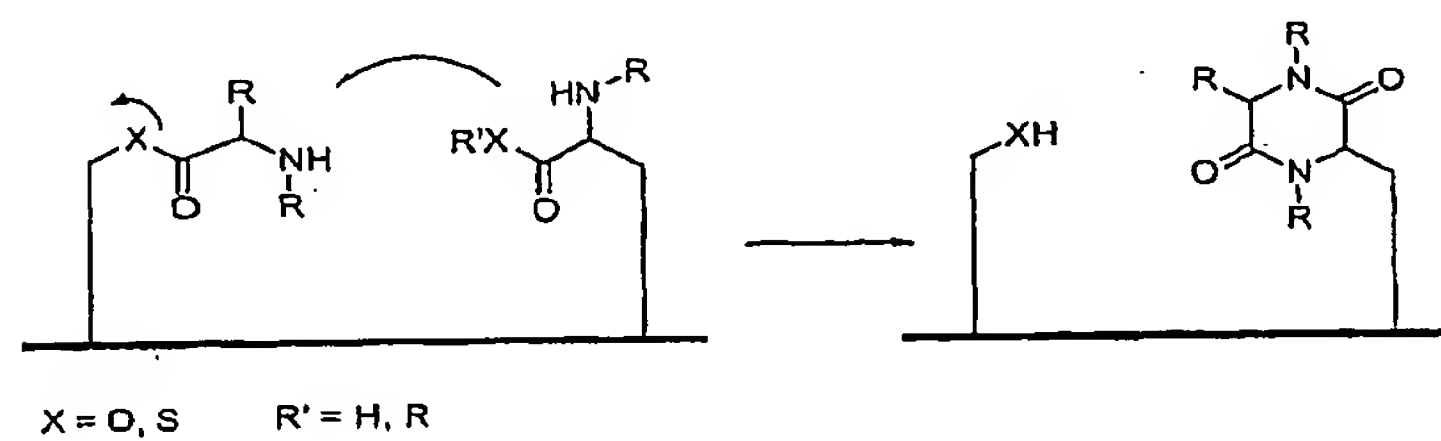


H. Acylation

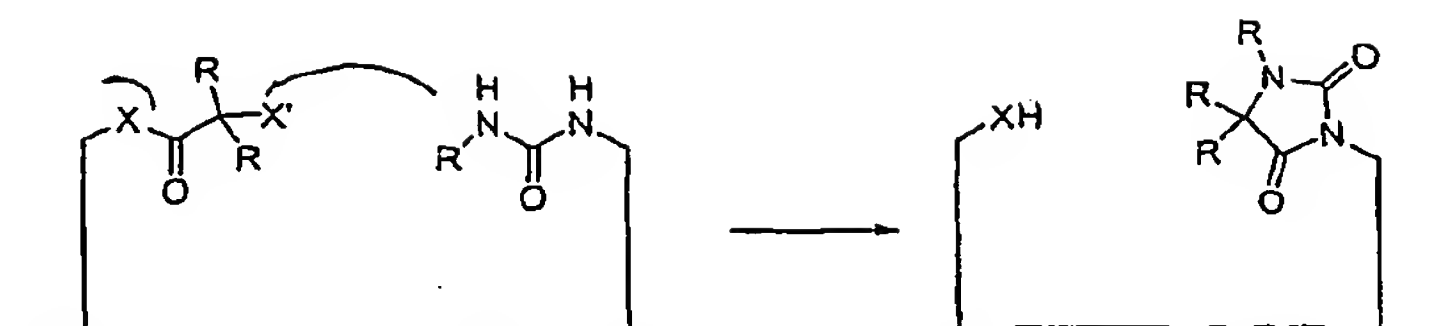
Phthalhydrazide formation by reaction of Hydrazines and Phthalimides

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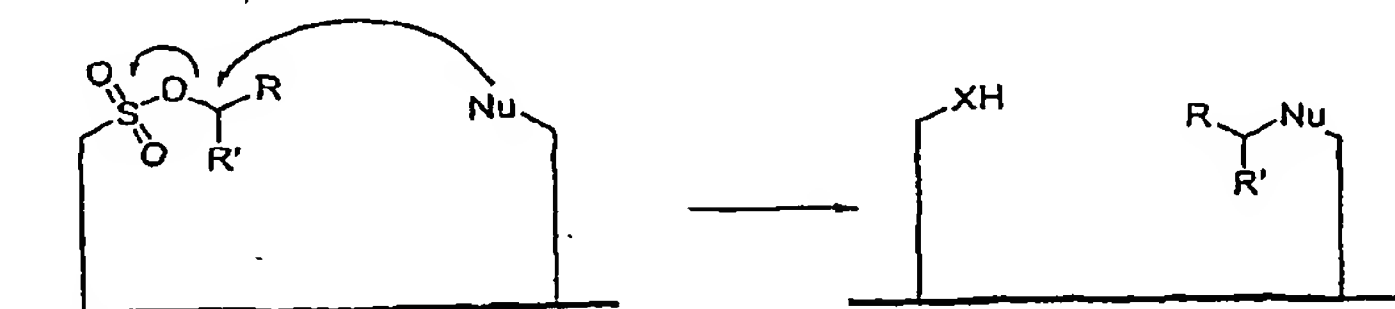
**I. Acylation****Diketopiperazine formation by reaction of Amino Acid Esters****J. Acylation****Hydantoin formation by reaction of Urea and α -substituted Esters****SUBSTITUTE SHEET (RULE 26)**

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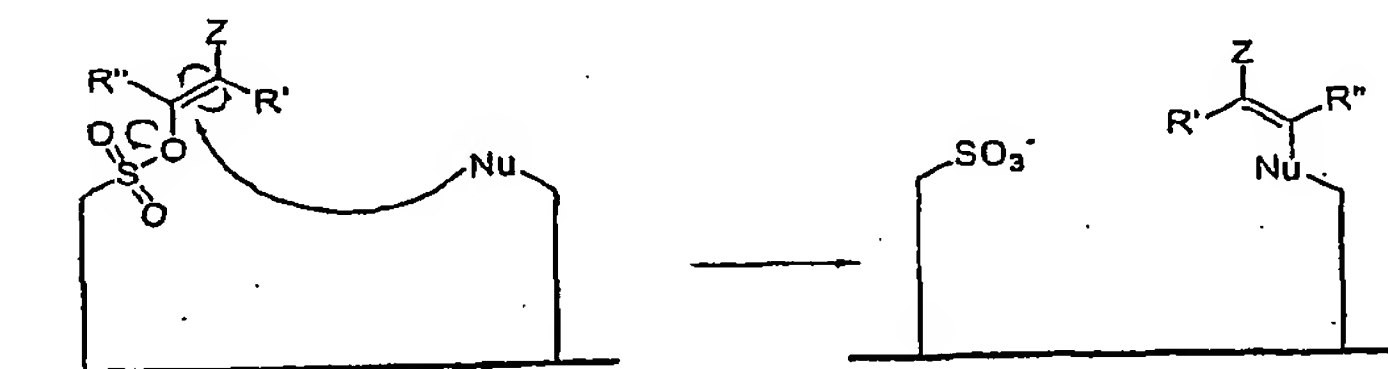
$X = O, S$ $X' = \text{Hal, OTos, OMs, etc.}$

K. Alkylating monomer building blocks - principle
Alkylated compounds by reaction of Sulfonates with Nucleophiles



$\text{Nu} = \text{Oxygen-}, \text{Nitrogen-}, \text{Sulfur- and Carbon Nucleophiles}$

L. Vinylating monomer building blocks - principle



$Z = \text{CN, COOR, COR, NO}_2, \text{SO}_2\text{R, S(=O)R, SO}_2\text{NR}_2, \text{F}$
 $\text{Nu} = \text{Oxygen-}, \text{Nitrogen-}, \text{Sulfur- and Carbon Nucleophiles}$

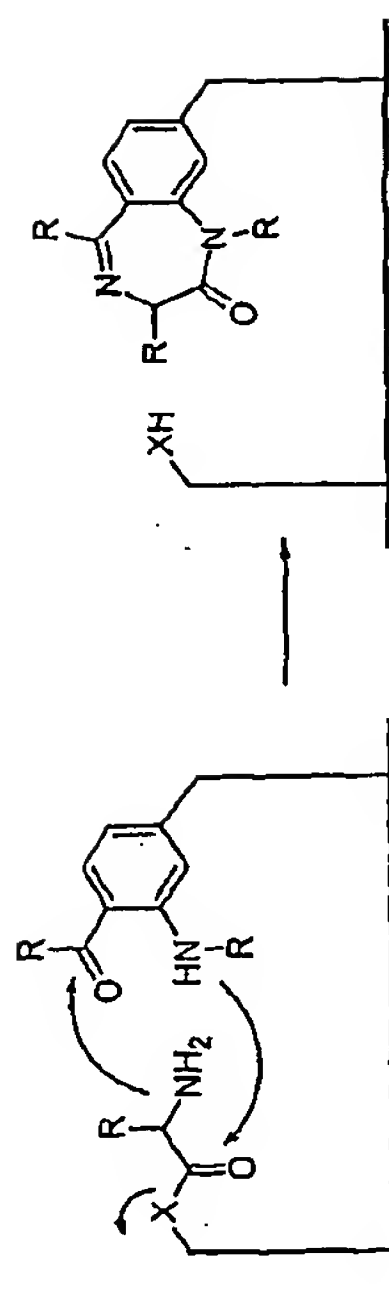
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M. Heteroatom electrophiles**Disulfide formation by reaction of Pyridyl disulfide with mercaptanes**

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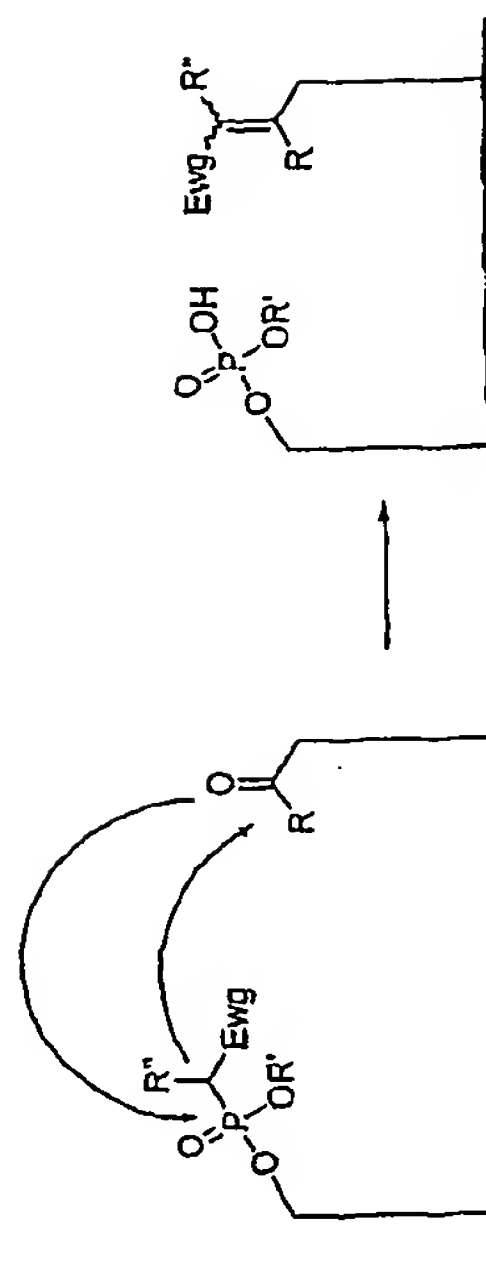
N. Acylation
Benzodiazepinone formation by reaction of Amino Acid Esters
and Amino Ketones



X = O, S

Addition to carbon-hetero multiple bonds

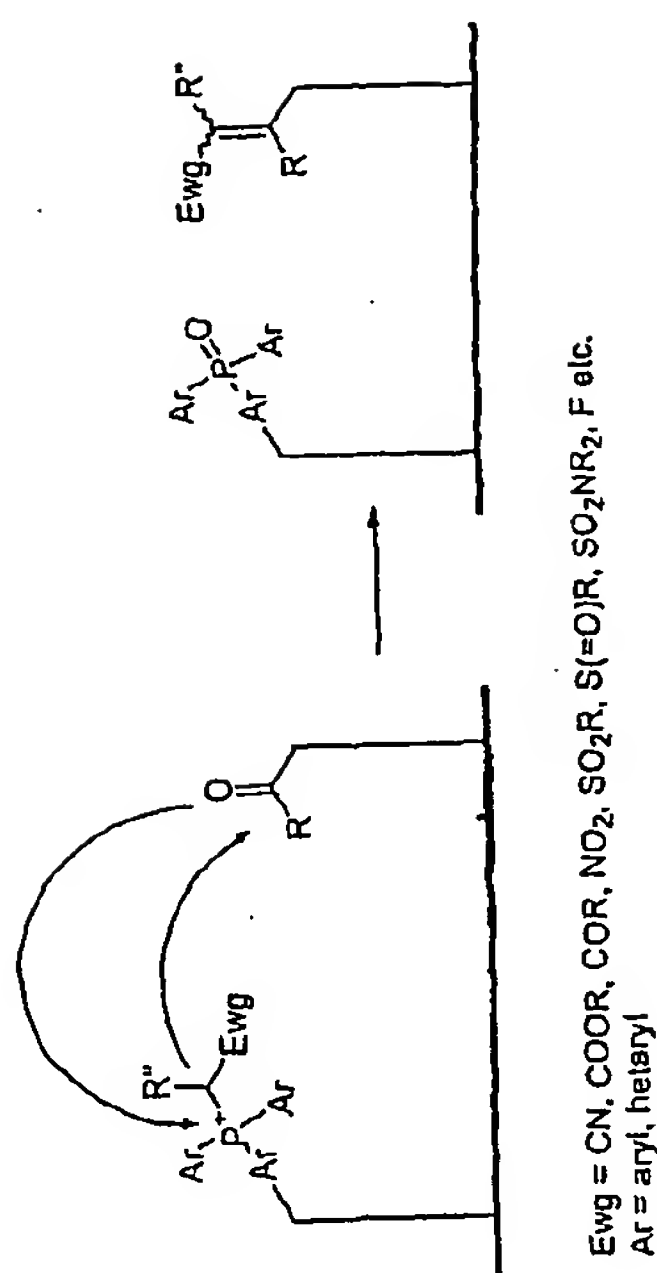
O. Wittig/Horner-Wittig-Emmons reagents
Substituted alkene formation by reaction of Phosphonates with Aldehydes or Ketones

Ewg = CN, COOR, COR, NO₂, SO₂R, S(=O)R, SO₂NR₂, F etc.

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P. Wittig/Horner-Wittig-Emmons reagents
Substituted alkene formation by reaction of Phosphonates with Aldehydes or Ketones

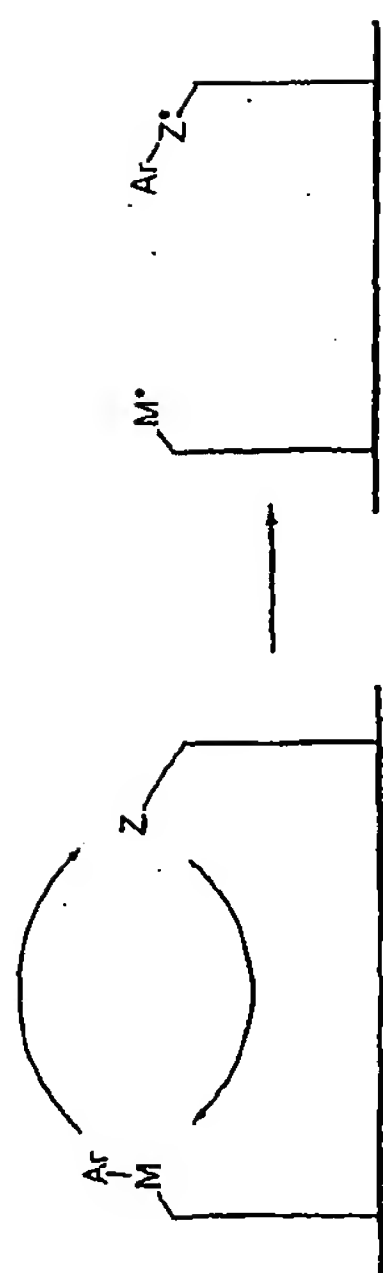


Transition metal catalysed reactions

Q. Transition metal cat. Arylations

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Z = haloaryl, haloaryl, ArOMs, ArOTf, ArOTos or NHR or OH or SH etc.

Z' = Aryl, hetaryl, NR or O or S etc

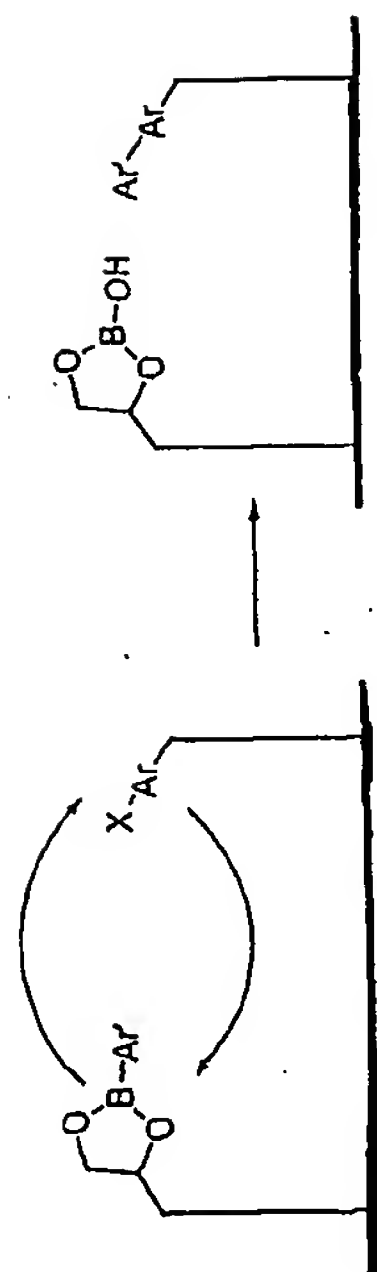
M = e.g. BR, BR₂, SnR₂ etc.

R = H, alkyl, aryl, hetaryl, OR, NR₂

M' = e.g. B(OH)R, B(OH)R₂, Sn(OH)R₂ etc.

R. Arylation

Biaryl formation by the reaction of Borates with Aryls or Heteroaryls

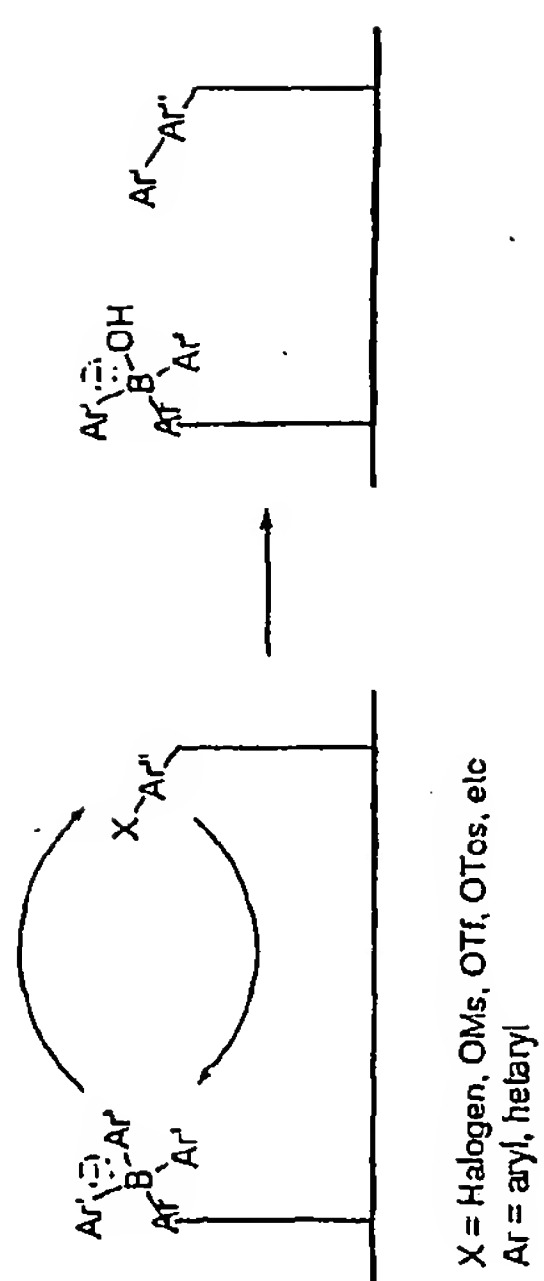


X = Halogen, OMs, OTf, OTos, etc

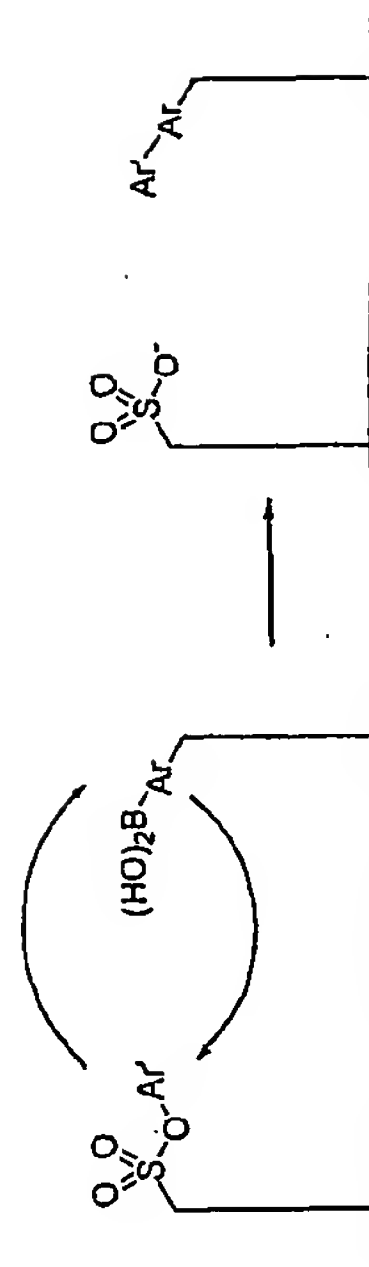
S. Arylation

Biaryl formation by the reaction of Boronates with Aryls or Heteroaryls

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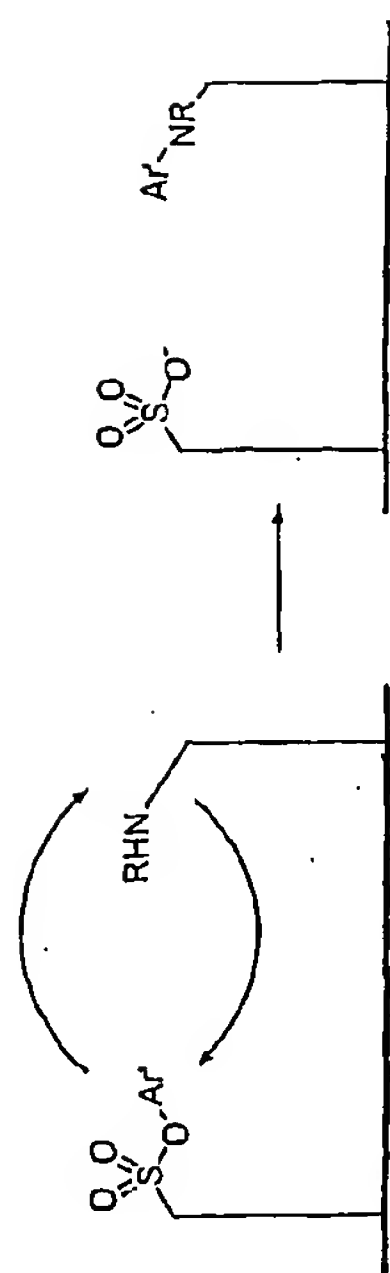


T. Arylation
 Biaryl formation by the reaction of Boronates with Aryls or Heteroaryls

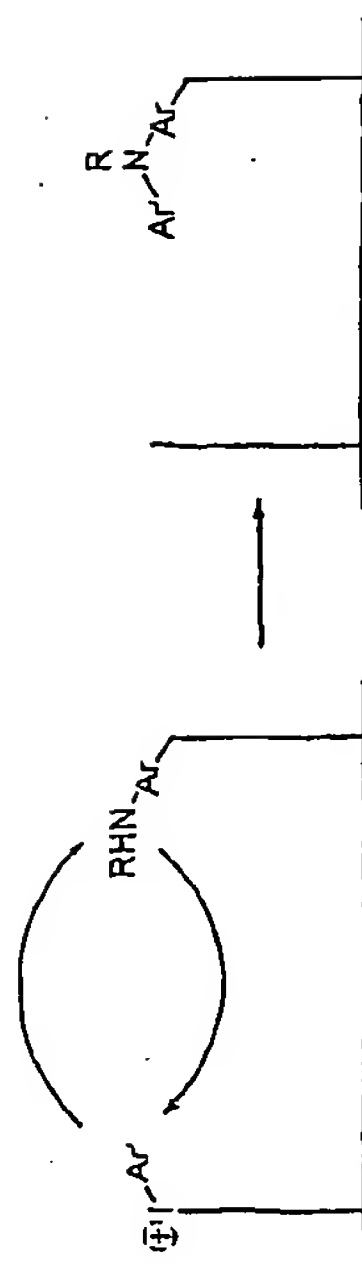


U. Arylation
 Arylamine formation by the reaction of amines with activated Aryls or Heteroaryls

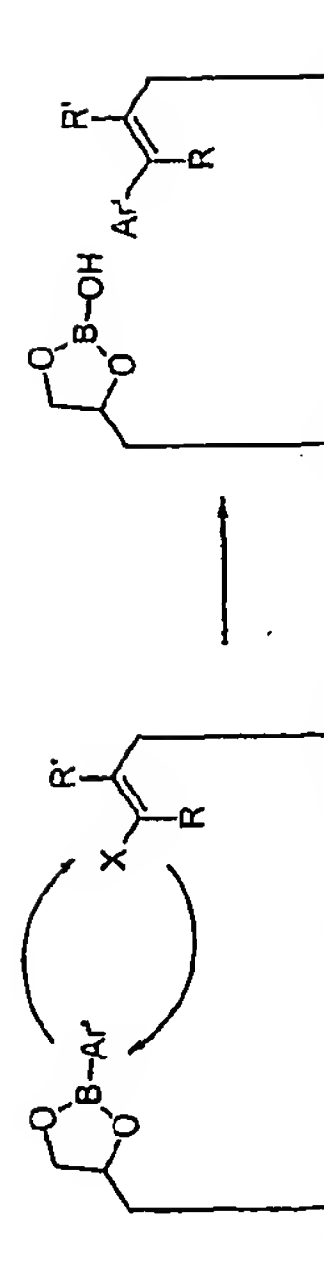
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V. Arylation
 Arylamine formation by the reaction of amines with hypervalent iodonium salts



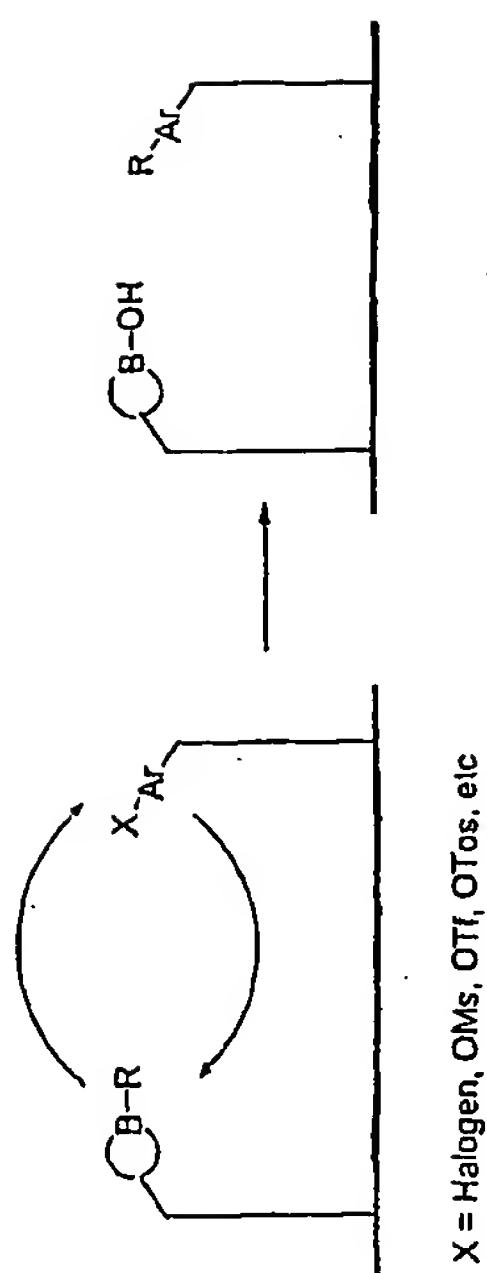
X. Arylation
 Vinylarene formation by the reaction of alkenes with Aryls or Heteroaryls



X = Halogen, OMs, OTf, OTos, etc

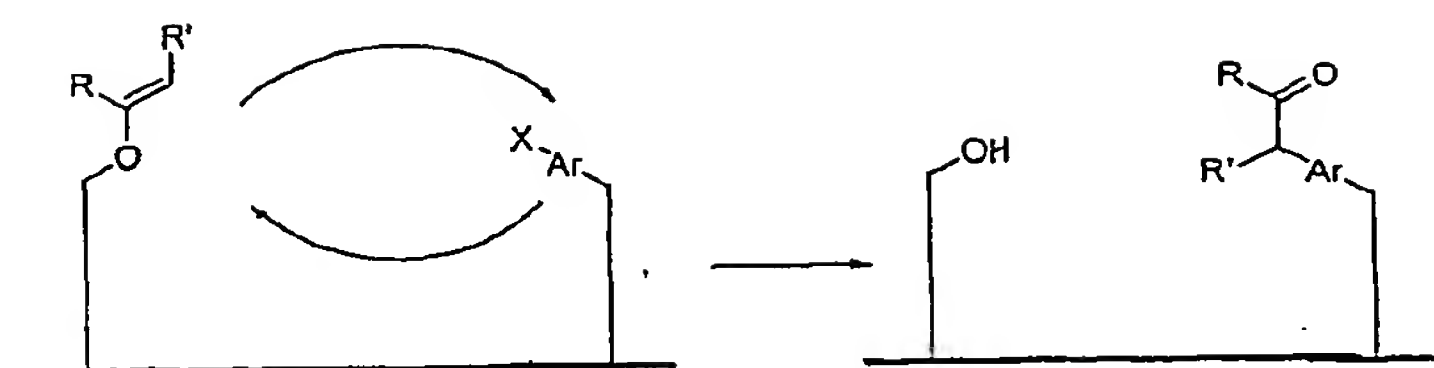
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Y. Alkylation
Alkylation of arenes/hetarenes by the reaction with Alkyl boronates



Z. Alkylation
Alkylation of arenes/hetarenes by reaction with enolethers

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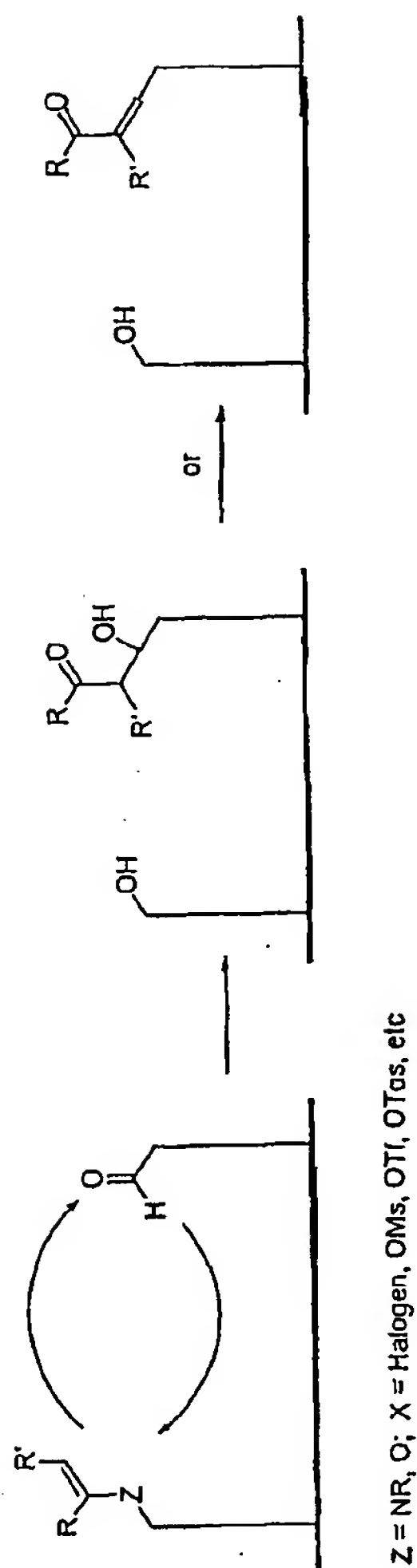
X = Halogen, OMs, OTf, OTos, etc

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Nucleophilic substitution using activation of nucleophiles

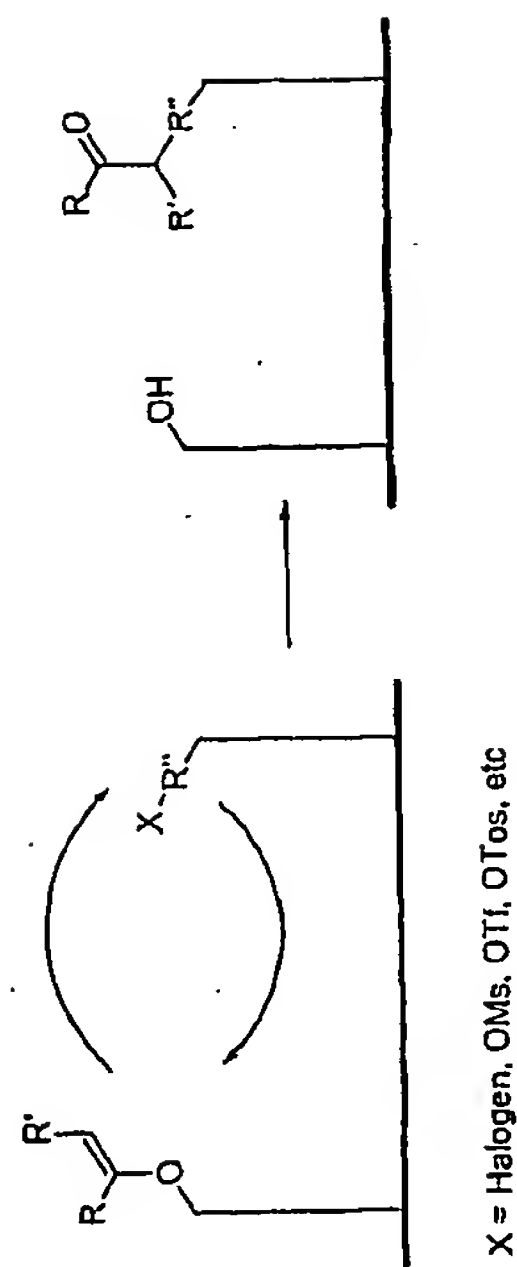
AA. Condensations

Alkylation of aldehydes with enolethers or enamines



AB. Alkylation

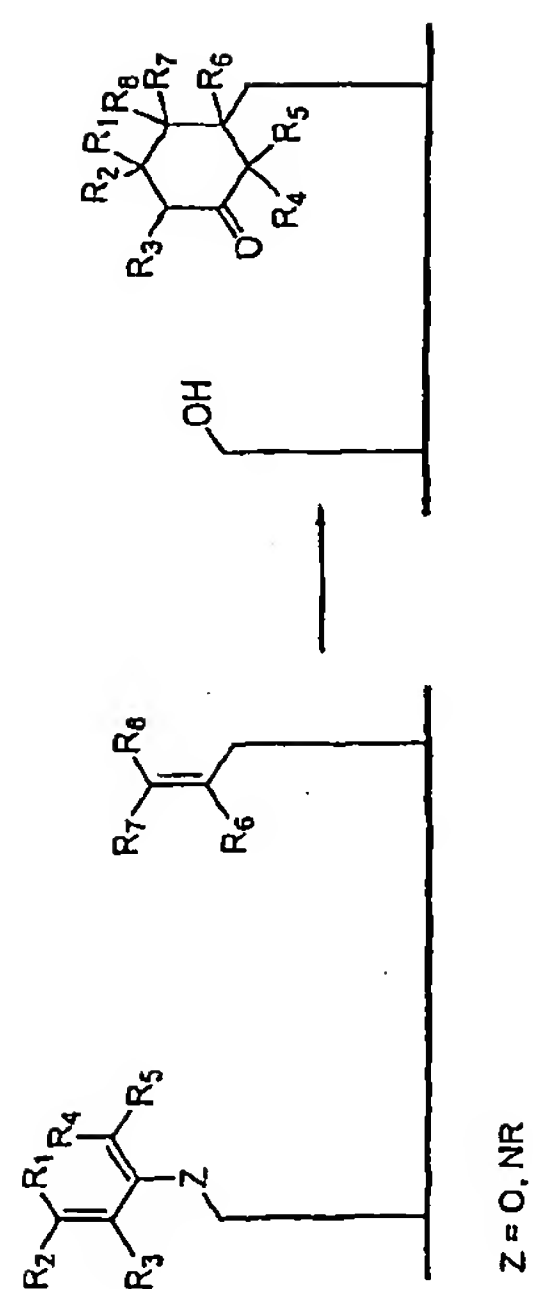
Alkylation of aliphatic halides or tosylates with enolethers or enamines



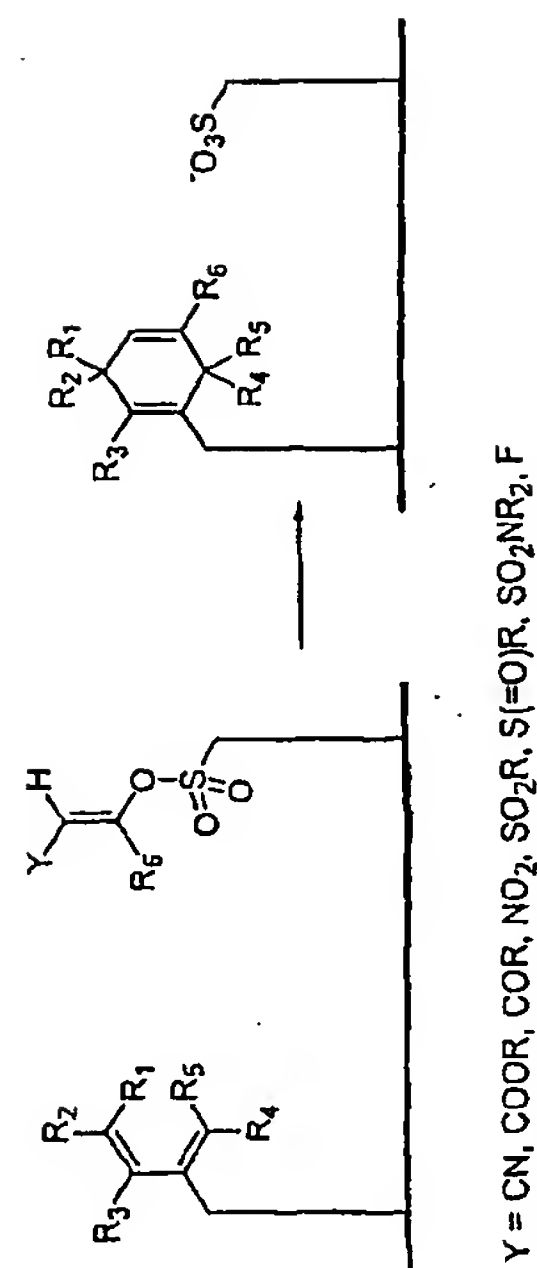
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Cycloadditions

AC. [2+4] Cycloadditions

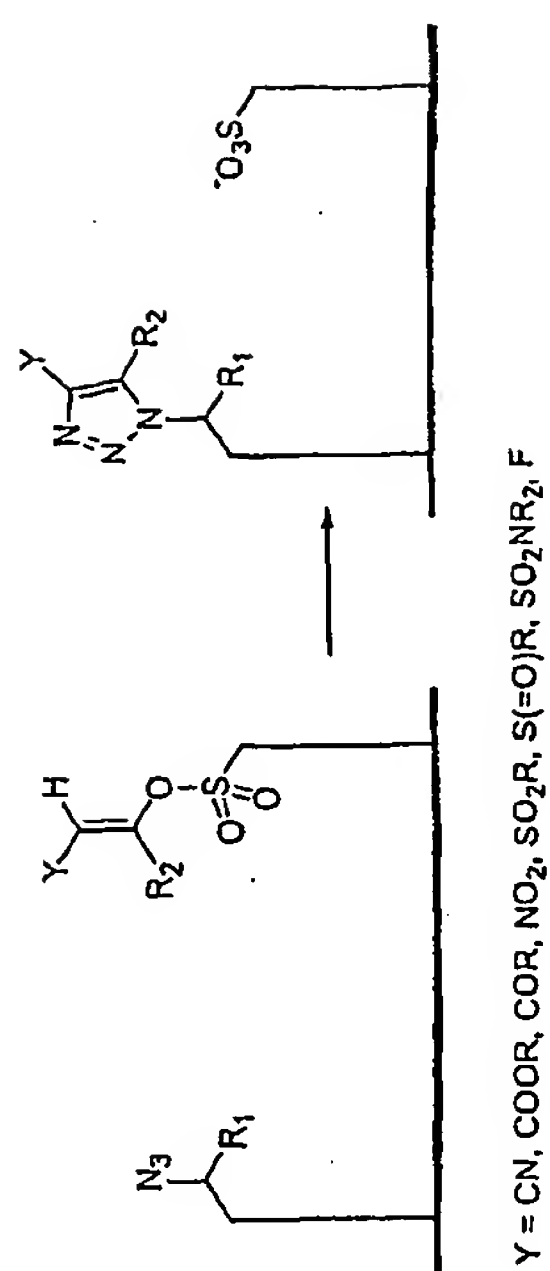


AD. [2+4] Cycloadditions

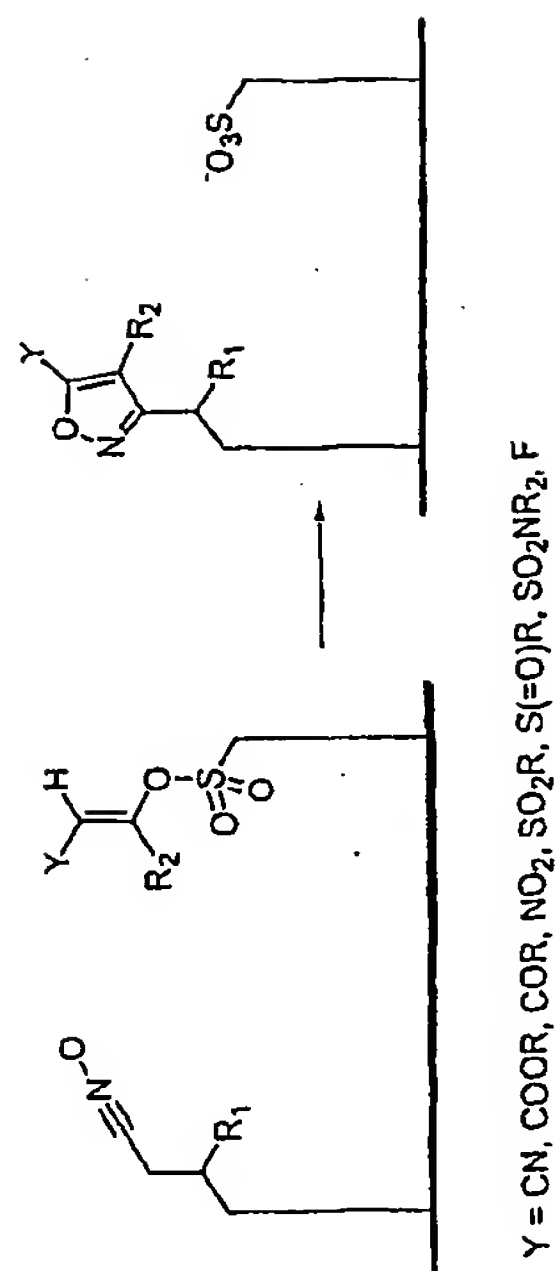


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AE. [3+2] Cycloadditions



AF. [3+2] Cycloadditions



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Figure 7. Pairs of reactive groups X,Y and the resulting bond XY.

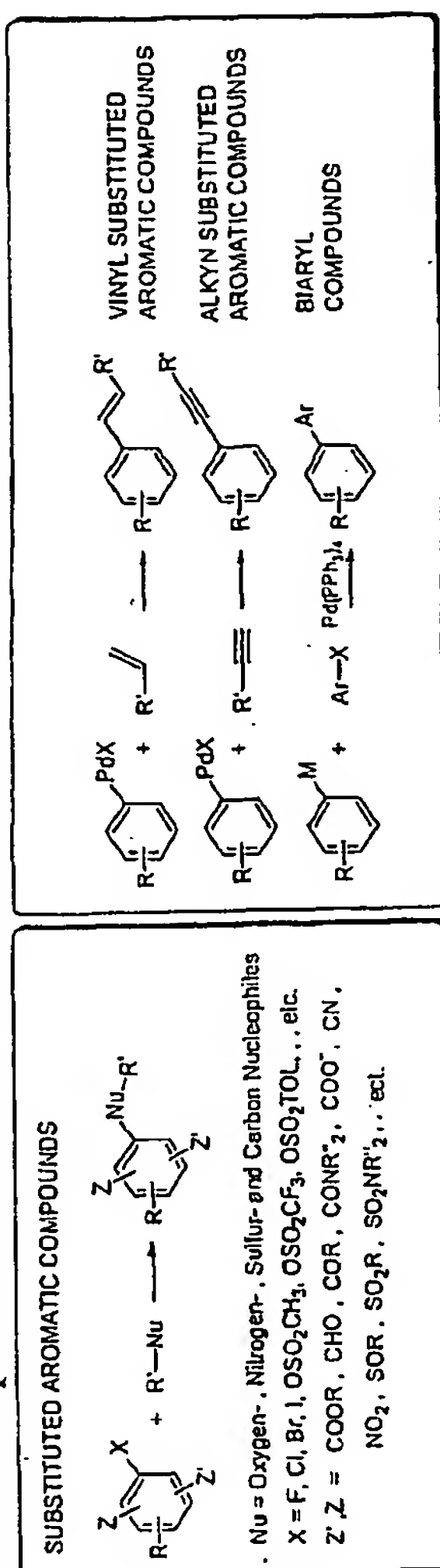
Nucleophilic substitution reactions

$R-X$	$+ R'-O-$	\longrightarrow	$R-O-R'$	ETHERS	$R-\overset{S}{\overset{O}{\parallel}}-O-R'$	$+ R''-NH_2$	\longrightarrow	$R-\overset{S}{\overset{O}{\parallel}}-HN-R''$	THIOAMIDES
$R-X$	$+ R'-S-$	\longrightarrow	$R-S-R'$	THIOETHERS	$R-\overset{O}{\parallel}-S-R'$	$+ R''-NH_2$	\longrightarrow	$R-\overset{O}{\parallel}-HN-R''$	AMIDES
$R-X$	$+ R'-NH_2$	\longrightarrow	$R-NH-R'$	sec-AMINES	$R-\overset{O}{\parallel}-S-R'$	$+ R''-NH_2$	\longrightarrow	$R-\overset{O}{\parallel}-HN-R''$	AMIDES
$R-X$	$+ R'-N-R'$	\longrightarrow	$R-N-R'$	tert-AMINES	$R-\overset{O}{\parallel}-S-R'$	$+ R''-NH_2$	\longrightarrow	$R-\overset{O}{\parallel}-HN-R''$	AMIDES
$R-X$	$+ R'-O-$	\longrightarrow	$R-O-R'$	β -HYDROXY ETHERS	$R-\overset{O}{\parallel}-S-R'$	$+ R''-NH_2$	\longrightarrow	$R-\overset{O}{\parallel}-HN-R''$	AMIDES
$R-X$	$+ R'-S-$	\longrightarrow	$R-S-R'$	β -HYDROXY THIOETHERS	$R-\overset{O}{\parallel}-S-R'$	$+ R''-NH_2$	\longrightarrow	$R-\overset{O}{\parallel}-HN-R''$	AMIDES
$R-X$	$+ R'-NH_2$	\longrightarrow	$R-NH-R'$	β -HYDROXY AMINES	$R-\overset{O}{\parallel}-S-R'$	$+ R''-NH_2$	\longrightarrow	$R-\overset{O}{\parallel}-HN-R''$	AMIDES
$R-X$	$+ R'-O-$	\longrightarrow	$R-O-R'$	β -AMINO ETHERS	$R-\overset{O}{\parallel}-S-R'$	$+ R''-NH_2$	\longrightarrow	$R-\overset{O}{\parallel}-HN-R''$	AMIDES
$R-X$	$+ R'-NH_2$	\longrightarrow	$R-NH-R'$	AMIDES	$R-\overset{O}{\parallel}-S-R'$	$+ R''-NH_2$	\longrightarrow	$R-\overset{O}{\parallel}-HN-R''$	AMIDES
$R-X$	$+ R'-S-$	\longrightarrow	$R-S-R'$	AMIDES	$R-\overset{O}{\parallel}-S-R'$	$+ R''-NH_2$	\longrightarrow	$R-\overset{O}{\parallel}-HN-R''$	AMIDES

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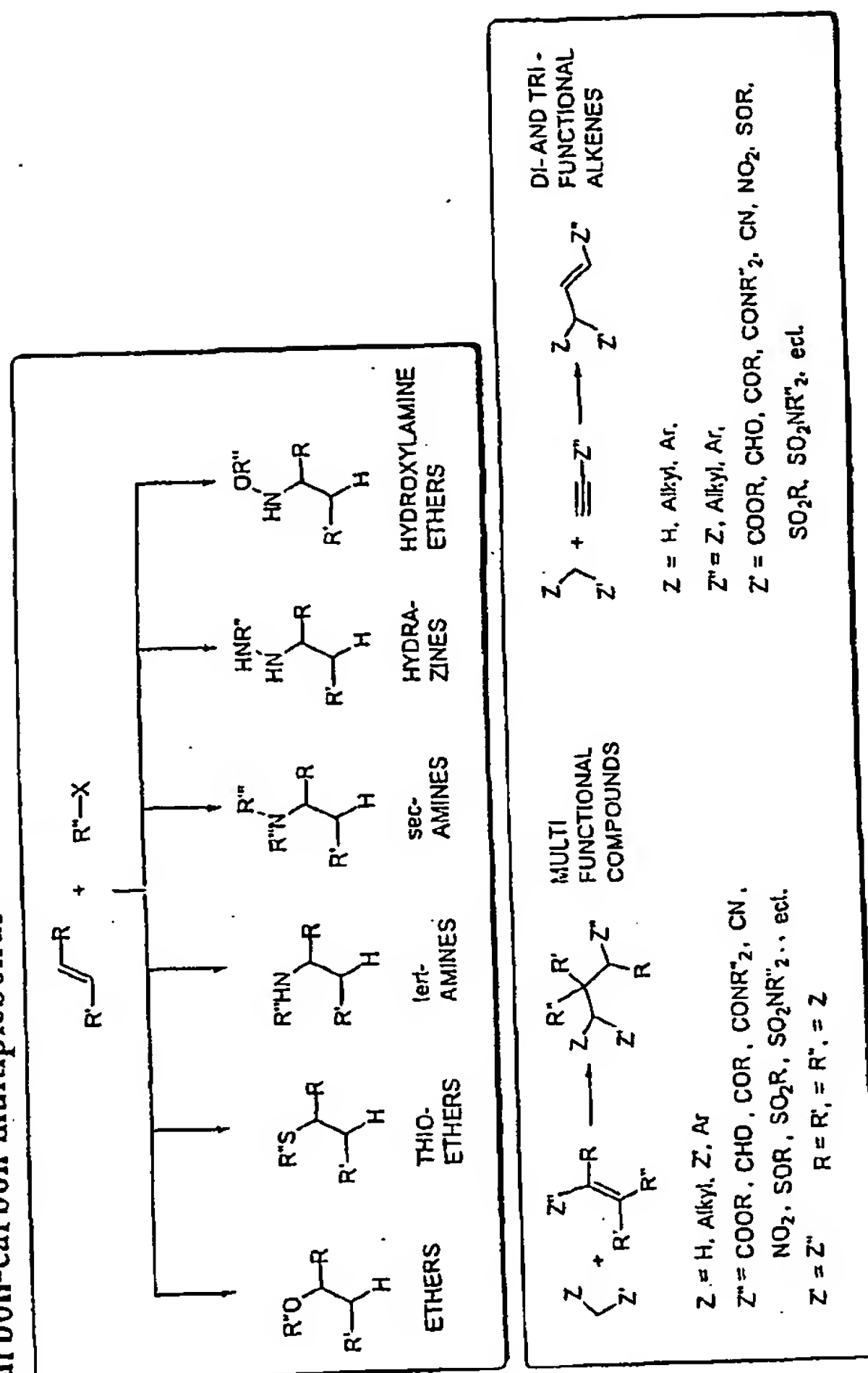
Aromatic nucleophilic substitution Transition metal catalysed reactions



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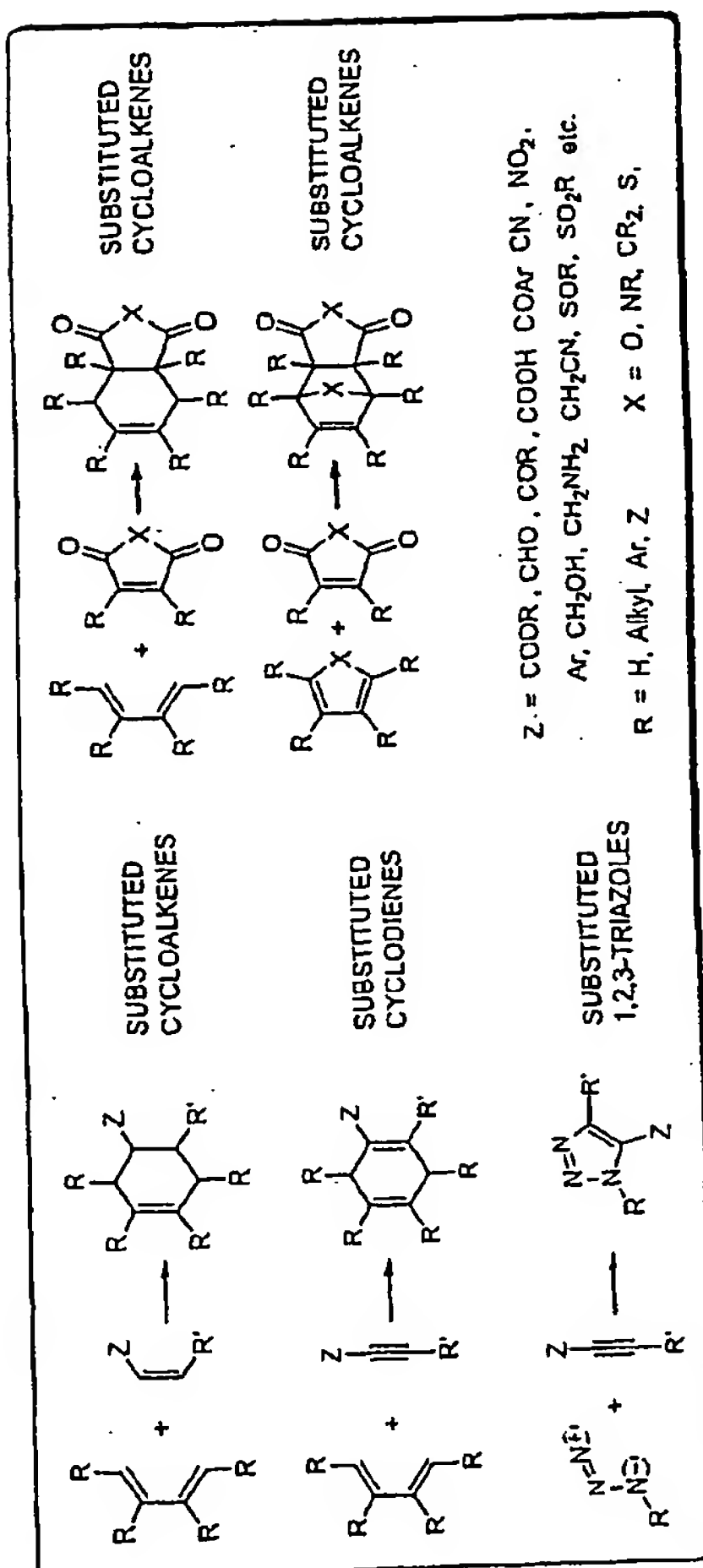
Addition to carbon-carbon multiple bonds



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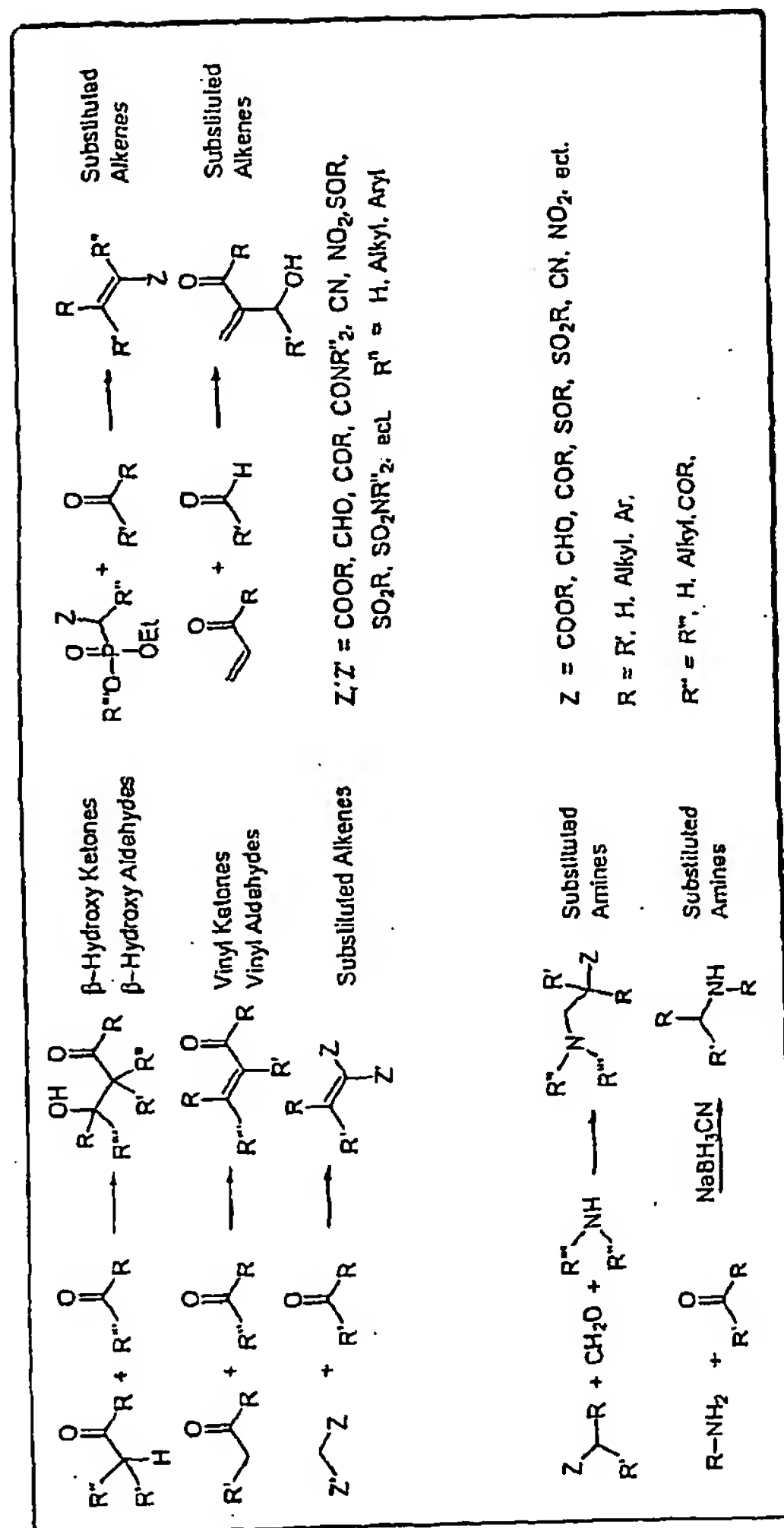
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Cycloaddition to multiple bounds



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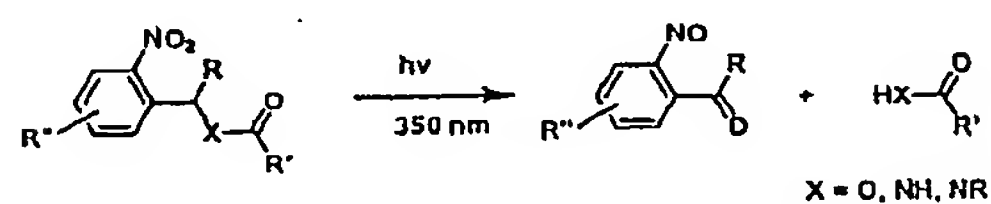
Addition to carbon-hetero multiple bonds.



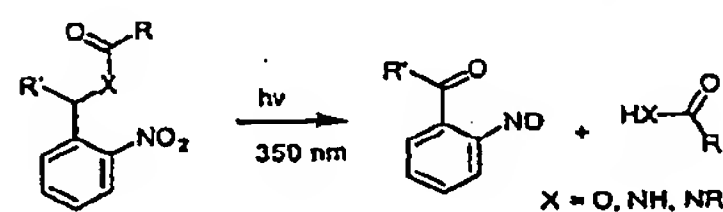
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Figure 8. Cleavable Linkers

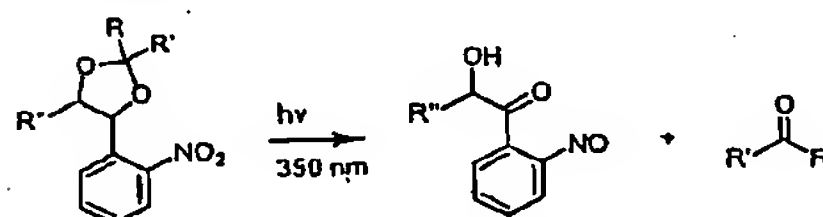
A. Linker for the formation of Ketones, Aldehydes, Amides and Acids



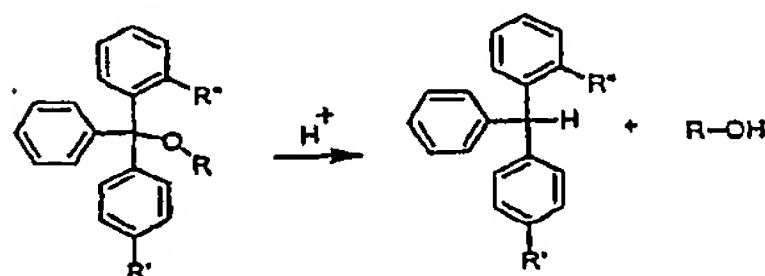
B. Linker for the formation of Ketones, Amides and Acids



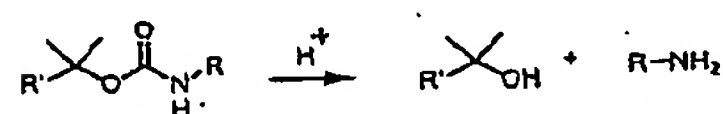
C. Linker for the formation of Aldehydes and Ketones



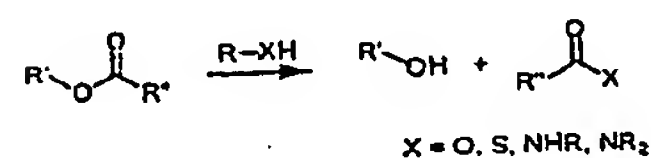
D. Linker for the formation of Alcohols and Acids



E. Linker for the formation of Amines and Alcohols

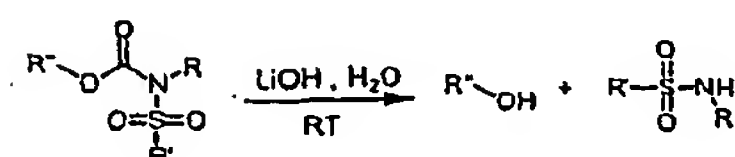


F. Linker for the formation of Esters, Thioesters, Amides and Alcohols

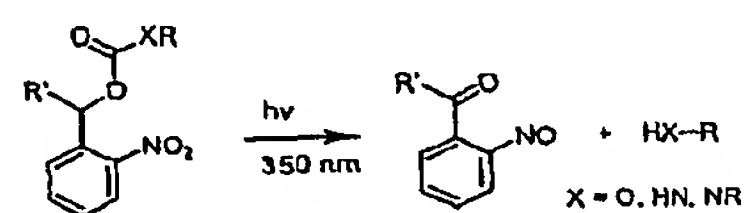
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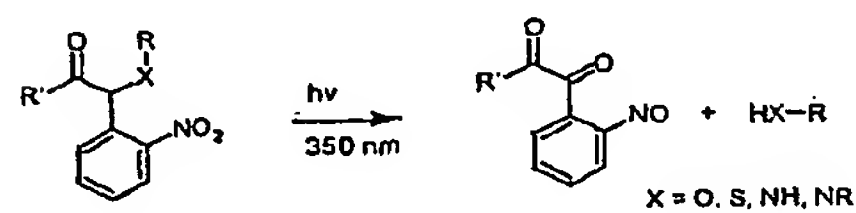
G. Linker for the formation of Sulfonamides and Alcohols



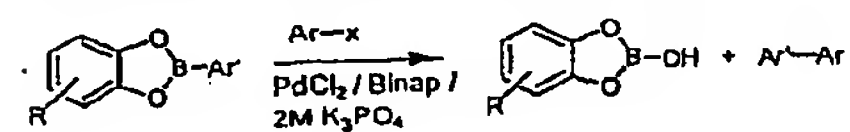
H. Linker for the formation of Ketones, Amines and Alcohols



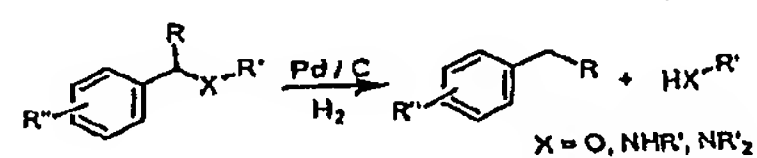
I. Linker for the formation of Ketones, Amines, Alcohols and Mercaptanes



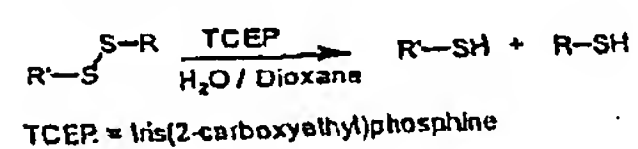
J. Linker for the formation of Biaryl and Biheteraryl



K. Linker for the formation of Benzyles, Amines, Anilins, Alcohols and Phenols



L. Linker for the formation of Mercaptanes



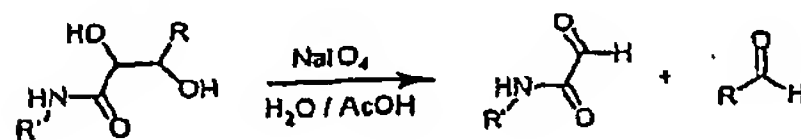
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M. Linker for the formation of Glycosides



N. Linker for the formation of Aldehydes and Glyoxylamides



O. Linker for the formation of Aldehydes, Ketones and Aminoalcohols

